

donors on GvHD and relapse development or posttransplant mortality.

**CONCLUSION:** The use of RIC is probably associated with less expressed inflammation (e.g. gastrointestinal tract) and in spite of allele G presentation (including homozygous form) it might lead to lower level of IL-6 and lower incidence of severe GvHD. In contradistinction to previously published analyses of patients allografted after standard myeloablative regimens, the assessment of this cohort with the frequent use of RICs (59%) failed to prove IL-6 gene polymorphism to be a universal predictor of posttransplant outcome in such circumstances.

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### MAJOR ABO BLOOD GROUP MISMATCH INCREASES THE RISK FOR GRAFT FAILURE AFTER UNRELATED DONOR HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Two hundred and twenty-four patients with leukemia transplanted with an unrelated donor between 1991 and 2003 at Karolinska University Hospital were analyzed according to association between graft failure and ABO, RhD, MNSs and Kidd blood group antigen compatibility. Median age was 29 years (range 0-55). Two hundred patients and donor pairs were HLA-A, -B, and -DR identical, and 24 patients had an allele-level mismatched donor. Conditioning consisted of TBI or busulfan-based myeloablative conditioning. All patients received ATG. A bone marrow graft was given to 152 patients and 72 patients received peripheral blood stem cells. Most patients received GVHD prophylaxis with CsA and MTX.

**Results:** 135 (60%) patients received an ABO mismatched graft and 89 received an ABO matched graft. Of the mismatched grafts, 67 (30%) were major mismatched and 68 (30%) minor mismatched. A bidirectional mismatch was found in 16 (7%) cases. Graft failure (GF) was seen in 6 (2.7%) patients. In the multivariate analysis major ABO mismatch (OR 14.9, 95% CI 2.01-110,  $p=0.008$ ) and HLA-allele mismatch (6.42, 1.19-34.8,  $p=0.03$ ) was significantly associated to GF. In patients with and without major ABO mismatch the incidence of GF was 7.5% (5/67) and 0.6% (1/157) ( $p=0.02$ ), respectively. In patients with and without HLA allele-level mismatch, the incidence of GF was 8.3% (2/24) and 2.0% (4/200) ( $p=0.09$ ).

**Conclusion:** Using an ABO major mismatched graft increases the risk for graft failure after unrelated donor HSCT.

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### FLUDARABINE – ORAL BUSULFAN MYELOABLATIVE CONDITIONING FOR ALLOGENIC PERIPHERAL STEM CELL TRANSPLANTATION. A SINGLE CENTER EXPERIENCE IN COLOMBIA

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A regimen of busulfan and cyclophosphamide was standard conditioning regimen for allogeneic PBSC in our center for the last 10 years. To reduced toxicity related to high dose cyclophosphamide, we are using a regimen of fludarabine and oral busulfan.

Here we report clinical outcome in the first 11 patients treated. The conditioning regimen consisted of 30 mg/m<sup>2</sup> intravenous fludarabine daily, day -5 to -2, and oral busulfan given at 1 mg/kg 4 times a day every 6 hours from day -5 to -2. Cyclosporine and methotrexate were used for prophylaxis of GVHD in 9 patients and Cyclosporine plus mycophenolate in 2.

Diagnoses were: AML in 5; MDS, NHL, ALL, NPH 1 each, and CML in 2. The median patient age was 40 years (range, 17-59 years). Mobilized blood stem cells were obtained from HLA-compatible siblings. Engraftment was achieved in all but one patient, who had high risk MDS, received a second transplant after losing the first graft a year before, and died on day +34. At a

median follow up of 3.5 months (range 5.3-1.25) all other patients are alive (day 100 transplant related mortality 7%). The median time for neutrophil and platelet recovery were 10.9 (min +7, max +13) and 12 (min 0, max +15) days. There was no cardiac toxicity and hemorrhagic cystitis. Grade 1-2 and grade 3 mucositis occurred in 45% and 27% respectively. Of 10 evaluable patients 7 had acute GVHD grade 1-2 and 1 grade 3. 70% of patients became CMV+ and received pre-emptive therapy.

Fludarabine – oral busulfan has been well tolerated in standard conditioning regimen versus cyclophosphamide – oral busulfan, but longer follow up is needed to establish definitive conclusions.

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### REDUCED RISK OF RELAPSE IN PEDIATRIC PATIENTS AFTER DOUBLE UNIT CORD BLOOD TRANSPLANTATION? A SINGLE INSTITUTION EXPERIENCE

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Unrelated umbilical cord blood transplantation (UCBT) has become a standard therapeutic option for pediatric patients who may benefit from hematopoietic stem cell transplantation but lack an adequate HLA-identical related donor. UCBT has the advantages of rapid availability and presumably lower risk of severe, acute GVHD despite donor-recipient HLA disparity. Double-unit UCBT (DUCBT) extends access to transplantation for patients who were previously disqualified on the basis of low cell dose in a single unit. Recent studies report high engraftment rate, acceptable rates of severe acute GVHD and acceptable rates of transplantation-related mortality with DUCBT. (Barker Blood. 2005;105:1343-1347). It is unknown, however, whether patients with advanced hematological malignancies and patients with severe co-morbidities would benefit from DUCBT. DUCBT was given to 7 patients with advanced hematological malignancies (AML, n=3, refractory n=1, 2CR n=1, 3CR n=1, ALL, n=4; 1CR Ph+ n=1, 2CR Ph+ n=1, both MRD+, 2CR n=2). The males/female ratio was 5/2. Ages were 5.2-15 yrs (median 14 yr). Five of seven were non-Caucasian (71%). Co-morbidities included invasive fungal infection (n=3), acute pancreatitis (n=1), and bulbar paralysis (n=1). Conditioning regimens were FTBI and melphalan (n=3) and fludarabine with melphalan (n=4). Myeloid engraftment occurred in all patients. The median time to an absolute neutrophil count >500 was 34 days (range 26-74 days). Three patients remained platelet transfusion dependent after day 100. In the remaining 4 patients the median time to a platelet count >20,000 unsupported were 51 days (range 44-69 days). All patients (100%) experienced Grades II-III acute GVHD. There were no patients with Grade IV GVHD and no deaths from acute GVHD. Four patients developed extensive chronic GVHD of the skin only. The 100 day transplant related mortality was 0%. One patient died on day +200 from respiratory failure secondary to multiple recurrent viral infections (CMV, Parainfluenza type 3, and herpes simplex virus). None of the patient suffered relapse. The disease-free survival is 80% with a median day +405 post transplant (range 173-1126). The observation that DUCBT may be associated with a reduced risk of relapse in patients with high-risk leukemia deserves further evaluation. Larger studies will be needed to confirm the clinical observation and investigate what are the potential mechanisms by which DUCBT could mediate an anti-leukemic effect.

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### UMBILICAL CORD BLOOD TRANSPLANTATION USING NON-MYELOABLATIVE CONDITIONING: THE MEXICAN EXPERIENCE

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